Splenic Neutropenia in the Felty Syndrome

By H. E. Hutchison and W. D. Alexander

THE POSSIBILITY that overactivity of the spleen might cause neutropenia, mentioned by Bauer in 1899,1 was discussed at length by Frank2 who drew attention to the close association between splenomegaly of diverse etiology and neutropenia; that was in 1916, the year in which Kaznelson3 first reported rise of the platelet count following removal of the spleen in thrombocytopenia. Since then splenectomy for thrombocytopenia has steadily become more firmly established, as experience has proved its value, and as the type of case in which it is effective has been more closely defined. In striking contrast splenectomy for neutropenia is still hardly out of the experimental stage; Frank’s observations were not followed up and until Reissmann in 19384 and Wiseman and Doan in 19395 and 19426 described the “primary” form of splenic neutropenia, the possibility that splenectomy might be curative in certain cases of neutropenia was neglected. Perhaps such cases were obscured by the greatly increased incidence, beginning in the 1920’s, of neutropenia due to arsenicals and later to the amidopyrine analgesics which focused attention on drug sensitivity as a cause of neutropenia.

In recent years, however, there has been a revival of interest in overactivity of the spleen as a cause of neutropenia although uncertainty still exists regarding not only the cause of the hypersplenism but also the mechanism by which the neutropenia is brought about. Thus Doan and his associates8-11 are convinced that the cause lies in excessive sequestration and phagocytosis by the spleen, whereas Dameshek and his co-workers12-15 champion the belief that the spleen exerts an inhibitory effect on the production of neutrophils by the marrow; still other factors, e.g. immunologic, may well be concerned.

This paper describes the occurrence of chronic malignant neutropenia in a patient with Felty’s syndrome who improved greatly following splenectomy. Review of the published cases of splenic neutropenia reveals that the association with chronic arthritis, to which attention was recently drawn by Gauld,16 is more common than had generally been suspected, and suggests that some cases of so-called primary splenic neutropenia may be merely examples of an exaggerated form of Felty’s syndrome. Furthermore, review of the recorded histologic findings in splenic neutropenia permits the recognition of two forms of the disease and leads to the surprising conclusion that no single mechanism seems to be invariably concerned but that either that suggested by Doan or that suggested by Dameshek may have been at work in individual cases.

From the Department of Pathology, The University and Western Infirmary of Glasgow and the Department of Medicine, Western Infirmary, Glasgow, Scotland.

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Mrs. M. P., a housewife, aged 59 years, was first admitted to the Western Infirmary, Glasgow, on July 7, 1950 complaining of weakness and sweating. She had been well until 1949, apart from chronic rheumatoid arthritis which had caused slight disability for some twenty years. The metacarpophalangeal joints of both hands were the only ones significantly affected; there had been no evidence of activity in recent years. Since 1949 she had been troubled by recurrent septic sores affecting the nose, mouth, throat, and conjunctivae. There was no history of the use of analgesics other than aspirin or of exposure to hemotoxic agents, but as a precaution the position was explained to her and she was forbidden all medicines except those prescribed by the hospital; no improvement resulted. During the next two and one-half years she was readmitted seven times; three admissions were for the treatment of infections, three because blood transfusions were thought advisable for granulocytopenia, and one to try the effect of ACTH on the white cell count.

On several occasions finger pricks for blood counts became septic and on one occasion lymphangitis followed. In April 1951 she was dangerously ill with a large abscess in the buttock which developed during a course of penicillin injections for severe laryngitis. In 1952 she had pneumonia.

Pathologic pigmentation of the skin was absent, and no tendency to excessive bruising or hemorrhage following injury has been observed. The lymphatic glands have never been palpable.

Repeated blood examinations showed persistent leukopenia and a mild normocytic normochromic anemia. Between March 1951 and February 1953, when splenectomy was undertaken, twenty-five white counts were carried out. In spite of the infections mentioned the count, usually between 1000 and 2000, was always below 3000/cu. mm. except on one occasion when it was 4000. The numbers of polymorphs varied between 0 and 730/cu. mm.; thus the neutropenia, while it varied in severity, was constantly present. The proportion of polymorphs having a nonfilamented nucleus (group 1, Cooke) was very high, and varied between 70 and 80 per cent.

The sternal marrow was examined eight times during the three years she was under observation prior to operation. Both smears and histologic sections of the marrow

<table>
<thead>
<tr>
<th>Table 1.—Myelograms</th>
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<tbody>
<tr>
<td>Cell Types (%)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Segmented neut. polys</td>
</tr>
<tr>
<td>Nonseg. neut. polys</td>
</tr>
<tr>
<td>Eosinophile polys</td>
</tr>
<tr>
<td>Basophile polys</td>
</tr>
<tr>
<td>Neut. metamyelocytes</td>
</tr>
<tr>
<td>Eosin. metamyelocytes</td>
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<tr>
<td>Neut. myelocytes</td>
</tr>
<tr>
<td>Eosin. myelocytes</td>
</tr>
<tr>
<td>Promyelocytes</td>
</tr>
<tr>
<td>Myeloblasts</td>
</tr>
<tr>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Hemoctoblasts</td>
</tr>
<tr>
<td>Proerythroblasts</td>
</tr>
<tr>
<td>Early normoblasts</td>
</tr>
<tr>
<td>Intermed. normoblasts</td>
</tr>
<tr>
<td>Late normoblasts</td>
</tr>
<tr>
<td>Plasma cells</td>
</tr>
<tr>
<td>Monoocytes</td>
</tr>
<tr>
<td>Leukoerythropgenic ratio</td>
</tr>
</tbody>
</table>
were prepared from the aspirates and the significant findings were essentially the same throughout the entire period. There was a well marked hyperplasia, as was clearly shown in section by the replacement of fat by hemopoietic tissue. Both myeloid and erythroid elements were increased and the leukoerythrogenetic ratio, as the preoperative myelograms (table 1) show, was slightly reduced. In the myeloid series the significant abnormality was the almost complete absence of segmented neutrophils, though band forms and other still less mature types of granular cell were quite numerous. It is interesting to note that the eosinophils were normally segmented. In the earlier samples no abnormality in the maturation of the red cell precursors was observed but in the immediately preoperative sample an occasional macronormoblast could be found. Megakaryocytes were present in normal numbers in all samples.

Treatment of infections was with fresh blood transfusion and antibiotics. Pentamidine, ACTH in daily dosage of 100 mg, for five days, pyridoxine, folic acid, and other vitamin preparations, including riboflavin, failed to raise the white cell count or alter the marrow picture and did not diminish the incidence of infection. Iron was without effect on the anemia. The possibility of splenic neutropenia had been fully considered but in the absence of splenomegaly the evidence was incomplete and splenectomy did not seem justified at this time.

In February 1953 the patient was admitted for reassessment. For the first time the spleen could be palpated though only on full inspiration. Blood examination at this time showed: Hb. 10.9 per cent, R.B.C. 3.7 million/cu. mm., P.C.V. 32.7 per cent, M.C.H.C. 33.3 per cent, reticuloocytes 1 per cent, icteric index normal. Platelet count 92,000/cu. mm. Bleeding time 3 min., clotting time 6 min., clot retraction normal. Red cell fragility normal. Direct Coombs' test negative. The patient's serum failed to sensitize a representative test panel of red cells. W.B.C. 1700/cu. mm. Neut. 221, lymph. 1139, monos. 238, eos. 102/cu. mm. The epinephrine test failed to show evidence of sequestration of white cells by the spleen. Liver function tests gave thymol turbidity 8 units, thymol flocculation + 3 units. The serum bilirubin was 0.2 mg. per cent.

Splenectomy was advised but had to be postponed for ten days because of buccal ulceration and fever. The operation was carried out by Professor Illingworth on Feb. 26, 1953 without special difficulty. Before removal of the spleen samples of blood were secured from the splenic artery and vein to see whether evidence could be obtained regarding the phago-

![Splenectomy](image)

**FIG. 1.—Rise in white blood cells following splenectomy.**
Examination of the Spleen

Immediately the spleen was removed impression preparations were taken from the cut surface and an attempt was made to perfuse a portion of the organ since the removal of the blood permits a more precise examination of the parenchyma and thus a better appreciation of the activity of phagocytosis by the sinus-lining cells. The organ weighed 900 Gm., was of normal consistence and neither the external nor the cut surface showed any abnormality. The Prussian blue reaction was strongly positive. On histologic examination of both perfused and nonperfused areas the most striking feature was the accumulation of iron chiefly in hypertrophied sinus-lining cells but also in scattered cells in the pulp and as an encrustation of some trabeculae. Owing to marked hyperplasia of the germinal centers of the Malpighian bodies the lymphoid tissue was much more prominent than might have been expected for the patient's age (fig. 2). The red pulp was congested but not to the extent seen in acholeus jaundice. No extramedullary hemopoiesis was present but small groups of plasma cells were seen and occasional eosinophils. No evidence of excessive phagocytosis of white cells was found either in the imprint preparations or in the paraffin sections. In addition, frozen sections stained by the peroxidase method confirmed the absence from the spleen of abnormally large numbers of polymorphs (fig. 3). The number of granular cells present was indeed less than is commonly seen in normal spleens removed following trauma. There was therefore no evidence that the spleen was overactive in destroying these cells either by lysis or by phagocytosis.

Following the operation the patient's general condition improved markedly though the arthritis was unchanged. Six weeks later the Hb. had increased to 86 per cent (12.7 Gm.) and it has remained at that level. She has increased 7 Kg. in weight, and has been able to

Fig. 2.—Spleen showing numerous hyperplastic lymph follicles. The dark granules are hemosiderin. Hematoxylin and eosin, X 70.
Splenectomy in the Felty syndrome

Fig. 3.—Oxydase reaction. X 70. (A) Spleen from present case. (B) Spleen from malignant neutropenia. (C) Spleen from acquired hemolytic anemia without neutropenia.

enjoy a summer holiday for the first time in years. She remarked spontaneously that whereas minor scratches on the hands resulting from housework had formerly "always become septic," now they healed rapidly without suppurating. Ulceration in the mouth, throat, or other site has not recurred.

A sample of sternal marrow secured eight months after operation presented a striking contrast with the previous findings. Histologic sections showed that the hyperplasia had disappeared and a differential count on films revealed a substantially normal proportion of segmented polymorphs (see table 1). The leukocythrogenic ratio was now normal but there was an increased proportion of eosinophils such as is sometimes found in Felty's syndrome. Erythropoiesis was normoblastic. Over eleven months after operation: Hb. 13.2 Gm. per cent, P.C.V. 39.7 per cent, M.C.H.C. 33 per cent, W.B.C., 3800, cu. mm., neuts. 2552, lymphs. 2812, monos. 290, eos. 116. Approximately 50 per cent of the neuts. are Cooke type I. Platelets 188,000/cu. mm.

Discussion

The preoperative feature which suggested the diagnosis was the persistent paucity of segmented neutrophils in the marrow. Maturation arrest operating so late and of such long duration had never been observed by us in any previous case of neutropenia, e.g. in those due to drug sensitivity. In searching for an alternative explanation, overactivity of the spleen seemed a possibility, and the results of splenectomy have provided confirmation of this supposition. The presence of the mild anemia and thrombocytopenia shown by our patient is quite consistent with hypersplenism, which commonly affects all the formed elements of the blood though in varying degrees in different cases. The possibility that the anemia was hemolytic was investigated but no evidence to support this was found. It seemed probable therefore that the diminution in the red cell count, on which the normochromic anemia depended, was due to an inhibitory effect by the spleen on the production of red cells by the marrow. Whether the same mechanism was responsible for the thrombocytopenia, ex-
amination of the megakaryocytes did not permit us to say. Both the anemia and thrombocytopenia responded to splenectomy.

The failure of ACTH to raise the white cell count in our patient may have been due to the relatively short period of treatment, for others\textsuperscript{20-22} have obtained improvement with a lower dosage but over a longer period.

White cell counts were not carried out in the present case with sufficient frequency to allow us to state categorically whether the fluctuation in the neutrophils was cyclical or not. The patient, however, did not recognise any regular periodicity in the reappearance of symptoms and the temperature chart showed fever to be noncyclical. Furthermore, the marrow was examined on eight occasions, sometimes when she was febrile with an infection, at other times when she was nonfebrile and apparently well. On every occasion lack of segmented neutrophils was seen, never normal white cell production and never aplasia.

When the striking history of repeated infections is considered together with the laboratory findings and, above all, the curative effect of splenectomy which apparently restored normal white cell maturation the diagnosis of splenic neutropenia is fully substantiated.

A relationship between this case and Felty's syndrome can hardly be doubted. The patient had rheumatoid arthritis for many years, became leukopenic and eventually developed detectable splenomegaly; these constitute the diagnostic triad of Felty's syndrome in which commonly the arthritis is of longstanding duration and neither extensive nor severe, as was the case in our patient. In addition, the white cells in the peripheral blood showed the changes in the Cooke-Ponder count described by Collins\textsuperscript{20} in Felty's syndrome and the histologic findings, both in the enlarged spleen where there was lymphoid hyperplasia and plasma cell and eosinophil infiltration\textsuperscript{16, 19, 24-27} and in the marrow where there was apparently maturation arrest of granulocytes,\textsuperscript{9, 20, 21, 25, 28-32} were also entirely consistent.

Three lines of evidence indicate that the leukopenia of Felty's syndrome may be not only diagnostically significant but also concerned in the pathogenesis of symptoms. Firstly, cases in which excessive susceptibility to infection was a prominent feature are not infrequent.\textsuperscript{29, 30, 4, 49} Secondly, splenectomy is commonly,\textsuperscript{27, 31, 32, 35, 44, 49} though not always, beneficial.\textsuperscript{27, 41, 46, 47} Thirdly, when postmortem reports on Felty's syndrome are examined, evidence of agranulocytosis is readily found.\textsuperscript{24, 48-50}

There is therefore much to support our suggestion that this patient was an example of Felty's syndrome, in which an exaggerated degree of neutropenia dominated the picture. The possibility of such an association has been raised frequently in the past\textsuperscript{9, 33, 34, 35} in reports of similar cases but only Gauld\textsuperscript{13} has drawn attention to a possible association between arthritis and primary splenic neutropenia as recorded in the literature. When this possibility is examined in detail (see table 2) the remarkable fact emerges that, in approximately half of the cases recorded in the literature in which unequivocal benefit to the patient followed removal of the spleen for neutropenia, the patient was arthritic. The possibility that the arthritis might be the result of the neutropenia is excluded in most instances by the time relationship. Furthermore the joint changes do
not seem, from the rather scanty information available concerning them, to have presented features that would distinguish them from the ordinary form of rheumatoid arthritis met with in Felty's syndrome. Thus it does not seem justifiable to make an absolute distinction between Felty's syndrome with its mild leukopenia and a splenic neutropenic syndrome in which the neutropenia is sufficiently severe and prolonged to bring about the cardinal symptoms of fever, prostration, and excessive liability to infection. Felty's syndrome may develop into just such a neutropenic syndrome and since there is a high incidence of arthritis in splenic neutropenia it is obviously pertinent to suggest that some cases reported under the latter title might equally well be labeled Felty's syndrome. Indeed it seems quite unlikely that chance could account for the association of arthritis in ten of the twenty-one cases of splenic neutropenia in table 2, nor does the increased risk of drug neutropenia in arthritics, whose consumption of analgesics is likely to be considered greater than that of the general population, explain the association. All authors have been conscious of this possibility and have excluded it. In any case, splenomegaly is not usually detectable in drug neutropenia, nor does drug neutropenia become chronic.

When reported cases of splenic neutropenia are examined in regard to the neutropenic mechanisms apparently involved it will be seen (table 2) that the cases accompanied by arthritis do not form a single group; either the Doan or the Dameshek mechanism seems to have operated in an equal number of instances thus suggesting that cases of arthritis with neutropenia may not all be of the same nature. Indeed it seems that only those cases of arthritis with maturation arrest may have been examples of Felty's syndrome for since Steinberg first drew attention to the hyperplasia of the marrow, and Trolle and Trolle described the maturation arrest of neutrophils in Felty's syndrome numerous authors have confirmed these findings.

It is, however, difficult to assess, in many of the case reports in the literature, the true incidence of the crucial findings, namely, whether maturation arrest or phagocytosis was unequivocally operative. For example several authors state that no maturation arrest has been present while quoting only 2 per cent or even less of segmented neutrophils, with normal numbers of precursors; nor do they advance an alternative explanation to account for their finding, e.g. by the accelerated release into the blood and peripheral destruction of slightly immature granulocytes as is stated to occur in the antileukocytic immune body reaction of Moeschlin and Wagner. It is, however, appropriate to examine the marrow findings of our own case in the light of this postulated mechanism. When the preoperative and postoperative myelograms are compared it is evident that they coincide until the nonsegmented neutrophil stage is reached. The abnormality in granulopoiesis which has been ameliorated by splenectomy did not apparently operate before this level; and when the total numbers of segmented and nonsegmented neutrophils before and after operation are compared, close agreement is found. There is, therefore, since the splenectomy no evidence of retention of granulocytes which were, previous to operation, being prematurely released. On the contrary the findings seem to indicate that cells held up at the non-segmented stage before operation are now present as segmented forms i.e. their maturation is now proceeding more normally, but precise assessment of
TABLE 2.—Cases in which Splenectomy for Neutropenia Was Effective

<table>
<thead>
<tr>
<th>Author and Coauthors</th>
<th>Age &amp; sex</th>
<th>Arthritis</th>
<th>Periodicity</th>
<th>Marrow</th>
<th>Spleen</th>
<th>Followup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moore and Bierbaum</td>
<td>F-64 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Well 4 months; 25% eosinophils present</td>
</tr>
<tr>
<td>Nordenson and Roden</td>
<td>F-50 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>No phagocytosis</td>
<td>Sequestration and lysis</td>
<td>4 months later patient well and normal differential 14 months</td>
</tr>
<tr>
<td>Muether, et al.</td>
<td>F-31 yrs.</td>
<td>Absent</td>
<td>Cyclic</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Well; normal differential 14 months</td>
</tr>
<tr>
<td>Wiseman and Doan</td>
<td>F-38 yrs.</td>
<td>10 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>No return neutropenia 3 years 8/12</td>
</tr>
<tr>
<td>case 1</td>
<td>M-50 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>No return neutropenia 3 1/2 years</td>
</tr>
<tr>
<td>case 2</td>
<td>F-47 yrs.</td>
<td>7 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Continued well for 3 years 1/12</td>
</tr>
<tr>
<td>Langston, et al.</td>
<td>M-56 yrs.</td>
<td>6 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>2 years 9/12 cured</td>
</tr>
<tr>
<td>Salzer, et al.</td>
<td>F-59 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Well 6/12 later</td>
</tr>
<tr>
<td>Rogers and Hall</td>
<td>F-60 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>2 years normal. Developed typical rheumatoid arthritis 5 years after splenectomy</td>
</tr>
<tr>
<td>Auger, et al.</td>
<td>F-49 yrs.</td>
<td>7 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>2/12 cured</td>
</tr>
<tr>
<td>Kinsey and Bingham</td>
<td>M-55 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Apparent cure 2 1/2 years</td>
</tr>
<tr>
<td>McClean and Coleman</td>
<td>F-29 yrs.</td>
<td>1 yr.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Well 6/12 later</td>
</tr>
<tr>
<td>Mahner</td>
<td>F-24 yrs.</td>
<td>Absent</td>
<td>Arrest</td>
<td>No phagocytosis</td>
<td>Continued well</td>
<td>Remained well</td>
</tr>
<tr>
<td>case 2</td>
<td>F-47 yrs.</td>
<td>Absent</td>
<td>Arrest</td>
<td>No phagocytosis</td>
<td>Died 3/12 from nephritis</td>
<td></td>
</tr>
<tr>
<td>Peden</td>
<td>M-59 yrs.</td>
<td>15 yrs.</td>
<td>No comment</td>
<td>Hyperplasia</td>
<td>No phagocytosis</td>
<td>Improved 4/12, died 9/12</td>
</tr>
<tr>
<td>case 2</td>
<td>F-50 yrs.</td>
<td>10 yrs.</td>
<td>No comment</td>
<td>Hyperplasia</td>
<td>No phagocytosis</td>
<td>22/12 Excellent general condition</td>
</tr>
<tr>
<td>Weiss and Collins</td>
<td>M-19 yrs.</td>
<td>Absent</td>
<td>No comment</td>
<td>No phagocytosis</td>
<td>No phagocytosis</td>
<td>No neutropenia 4/12</td>
</tr>
<tr>
<td>Erf and Fry</td>
<td>F-55 yrs.</td>
<td>10 yrs.</td>
<td>Cyclic</td>
<td>Normal differential</td>
<td>Phagocytosis</td>
<td>Clinical cure, signs hematologic relapse 21/2 years</td>
</tr>
<tr>
<td>Fullerton and Duguid</td>
<td>M-62 yrs.</td>
<td>Absent</td>
<td>Cyclic</td>
<td>Arrest and aplasia</td>
<td>No phagocytosis</td>
<td>Clinical cure. Great hematologic improvement</td>
</tr>
<tr>
<td>Palumbo</td>
<td>M-50 yrs.</td>
<td>2 1/2 yrs.</td>
<td>No comment</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>2/12 cured</td>
</tr>
<tr>
<td>Monto, et al.</td>
<td>M-78 yrs.</td>
<td>Absent</td>
<td>Cyclic</td>
<td>No arrest</td>
<td>Phagocytosis</td>
<td>Marked clinical improvement 1 year</td>
</tr>
</tbody>
</table>

Since it is axiomatic that in neutropenia due to hypersplenism splenectomy must be followed by significant increase in neutrophils and by unequivocal improvement of the patient, the cases of Owen, Erf and Maier, Reimann, and Reznikoff are not included. Reimann’s case is not included as the spleen was not removed while both Natelson’s and Sandella’s patient died of lymphosarcomatosis. Of these six omitted cases, two had arthritis; all were cyclic.

The importance of immunologic factors must await the investigation of future cases.

In regard to the detection and assessment of the severity of sequestration and phagocytosis of neutrophils by the spleen many of the accounts are likewise
insufficiently detailed. Although much emphasis has been laid by Dous7 on the use of supravital staining methods not all are agreed on their value in splenic neutropenia and experience of supravital stains in other work in this laboratory does not suggest that their application would be of crucial importance in this disease. We would rather recommend, in addition to imprints, the use of the oxydase reaction on frozen sections for assessing the numbers of polymorphs in the spleen.

Few authors8, 25, 35, 39, 54 have reported comparisons of the numbers of white cells entering and leaving the spleen in cases of hypersplenism but the paradoxical result obtained in our own patient is not uncommon and emphasises the fallacies inherent in this investigation and the necessity for a scrupulous technic such as that used by Wright et al.9 for the collection of samples.

It should be emphasised that following splenectomy re-examination of the marrow is absolutely essential if complete assessment of the effect of the operation is desired. Clinical improvement is a practical yardstick but this throws no light on the mechanism of improvement and demonstration of a raised cell count following operation does little more; yet frequently these are the only results of splenectomy quoted. It is important, particularly in the so-called maturation-arrest type of case where there is no microscopic evidence of an active destructive process within the spleen, to obtain histologic evidence that its removal has rectified the abnormality in the marrow which the author had incriminated as the cause of the leukopenia.

Owing to these difficulties the number of cases available for analysis is comparatively small, accordingly, precise evaluation of the part played by Felty’s syndrome in the etiology of splenic neutropenia is not yet possible. Nevertheless, the association of arthritis, splenomegaly, and neutropenia, particularly when the marrow presents an appearance of late maturation arrest of granulocytes is too striking to be merely accidental. We believe that some cases of splenic neutropenia are, like our own, an exaggerated form of Felty’s syndrome. In reaching this conclusion, we do not wish to infer that Felty’s syndrome and rheumatoid arthritis are fundamentally different.27 They seem to differ simply in the degree of lymphoreticular involvement of tissues other than synovia. This variation, however, seems to have significance in determining whether a mild hypersplenism will lead to a merely diagnostic asymptomatic leukopenia, as in the ordinary form of Felty’s syndrome, or whether a severe hypersplenism will bring about a malignant and thus clinically significant neutropenia, and other less well defined effects. Felty17 observed in rheumatoids the splenic and lymphoid involvement and the neutropenia, but their significance was at that time not discernible. It does not seem justifiable merely on that account to withhold the use of the established eponym for cases which seem essentially similar to those which he, and many others after him, described; the disease has not altered, only the interpretation.

**Summary**

A 59 year old woman with chronic rheumatoid arthritis of twenty years’ duration developed chronic granulocytopenia and excessive susceptibility to
infection. Mild anemia and symptomless thrombocytopenia were also present. Eight marrow punctures over two and one half years all showed what appeared to be maturation arrest affecting the neutrophils so that segmented polymorphs alone were reduced in number. Throughout this period no form of therapy, including a five day course of ACTH, was effective in promoting normal granulopoiesis; only at the end of this period did the spleen become palpable. Splenectomy resulted in complete symptomatic cure which has been maintained for one year but hematologic cure was not fully obtained. It is believed that this case of splenic neutropenia is really an exaggerated form of Felty’s syndrome for the literature shows that malignant neutropenia is not rare in this disease. Furthermore analysis of the literature on splenic neutropenia reveals other cases of an essentially similar nature and the suggestion is put forward that Felty’s syndrome may be a fairly common cause of what has been regarded as primary splenic neutropenia. The possible integration of these findings with the immunologic leukopenic mechanism of Moeschlin is briefly discussed.

**SUMMARY IN INTERLINGUA**

Un femina de 59 annos de etate, qui suifreva depost 20 annos de cronic arthritis rheumatoide, disveloppava chronic granulocytopenia e excessive susseptibilitate a infectiones. Esseva etiam constatate un leve anemia e thrombocytopenia sin symptomas. Octo puncturas medullar, executate in le curso de duo e medie annos, monstrava sin exception un apparente arresto de maturacion que afficeva le neutrophilos de maniera que solo le segmentate polymorphos esseva numericamente reduceite. Durante iste periodo nulle forma de therapia—includente un curso de 5 dies de ACTH—sucedeva a promover un granulopoiese normal. Le splen deveniva palpabile solo al fin del periodo mentionate. Splenectomia resultava in un complete cura symptomatic. Isto se ha mantenite durante un anno. Del altere latere, le cura hematologic non esseva complete. Nos crede que iste caso de neutropenia splenic es in realitate un exaggerate forma del syndrome de Felty, proque le litteratura de neutropenia splenic revela altere casos de un essentialmente simile natura, e nos presenta le idea que le syndrome de Felty es possibilemente un satis frequente causa de lo que esseva considerate usque nunc como primari neutropenia splenic. Es presentate un breve discussion del possibilitate de coordinar iste constatationes con le mechanismo del corpores immuno-antileucocytic de Moeschlin.

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H. E. HUTCHISON and W. D. ALEXANDER

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